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Review

Tobacco and otorhinolaryngology: Epic and disaster

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ABSTRACT

More than 500 papers are retrieved from the PubMed database by the keywords "Tobacco" and "Otorhinolaryngology", none of which, however, is devoted to the history of a plant that has a major impact on our specialty and practice. The present report describes and analyzes how tobacco conquered the world, the conflicts it triggered and the impact it has had in our field over the past centuries.

1. In the beginning, revelation

In the late 15th century, the Spanish, followed by the Portuguese, came across tobacco in the New World. On October 28, 1492, on the eastern coast of Cuba, Columbus's crewmen noticed Arawaks inhaling the smoke of a dried herb. In a semantic shift, "tabaco" – which, in the native language referred to the pipe – was adopted by the Spaniards for the contents of the pipe, and then for the plant itself [1–4]. Eight years later, Alvarez Cobral landed in Brazil, and the historian Pêro vas da Caminha gave the name "*pétun*" to the tobacco that the Tupi in the region of Rio de Janeiro smoked and called "petyn" in their language [1–4].

The first tobacco seeds reached Spain in 1520, and the physician of King Phillip II was able to confirm the virtues the native Americans claimed for the plant: appetite suppressant, mood enhancer, psychostimulant and local anesthetic [1,2]. In 1550, the Spanish introduced tobacco in the Low Countries. The Ottoman Empire discovered it in 1560, Morocco in 1593 (via the Sudan, seeds having been exported to Africa by Portuguese merchants) [2]. Tobacco seeds were taken to Japan by Christian missionaries in 1596, while French Huguenot refugees "contaminated" the Holy Roman Empire [2].

Several individuals were involved in the subjugation of France. In 1552, André Thevet (Fig. 1), then chaplain of an expedition to found a colony in the bay of Rio de Janeiro, rediscovered "*pétun*" [1,2]. He was driven back to France in 1556 by an outbreak of plague and, among other curiosities, brought back seeds that he planted and grew near Angoulême [1,2]. A few years later, in 1561, Jean Nicot (Fig. 2), then French ambassador to Portugal, came into contact with "tabaco"; some say he planted seeds he had got from a Flemish merchant in the embassy garden in Lisbon, others that a Portuguese market-gardener supplied him with a powder of dried leaves [1,4]. He wrote to the Cardinal of Lorraine, who was close to the Queen of France: "I have come into possession of an herb of the Indies, marvelous and proven force against the *Noli Me Tangere* and fistulae despaired incurable by physicians and a singular prompt remedy to nausea. When so it shall have seeded I will dispatch the same to a gardener in Marmoustier and place some of the plant in a barrel to be replanted and maintained likewise as I have for the orange trees" [2]. According to historians, Catherine de' Medici and/or her son Francis II soothed their headaches with the plant, and the entire Court thus adopted this "Queen's herb" or "Catherinary herb", taken in the form of snuff [2,5]. In 1586, in his *Historia Generalis Plantarium*, the physician and botanist Jacques Daléchamps (Fig. 3) named in "Nicotiana", for Jean Nicot, much to the annoyance of Thevet, who expostulated: "I was the first in France that brought the seeds of this plant and also that planted and did name the same "herb of Angoulême". Since what time, a trifler, that never was of the voyage, some ten years after my return to this land, has given it his name!" [2].

In Virginia, as of 1610, Sir Walter Raleigh began tobacco farming with labor imported via the Triangular Trade between Europe, Africa and the Americas [2]. Thereafter, it spread throughout all strata of society. In France under Louis XIII, tobacco was selling for 12 *sous* a pound in the form of "carrots" that could be grated, chewed or crumbled for smoking [1] (to this day in France, tobacconists' shop-fronts are distinguished by a sign in the form of a long red lozenge, based on two "carrots" joined at their tops [2]).

Only in 1809 did Louis Nicolas Vauquelin, professor of chemistry at the Medical School of Paris, isolate a volatile alkaline active

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Fig. 1. André Thevet.

principle in tobacco leaf juice [5]. In 1828, Posell and Reimann, in the University of Heidelberg, purified this psychoactive substance, and named it *nicotine* [5]. Nicotine induces addiction and habituation and has insecticidal and fungicidal properties that protect the plant against insects and certain forms of parasitosis. It is toxic when ingested orally – a single cigar contains double the lethal dose of 40 to 60 mg – and its first proven use as a murder weapon dates from 1851 [5,6]. Its metabolism and interaction with dopamine were described in 1950 [1].

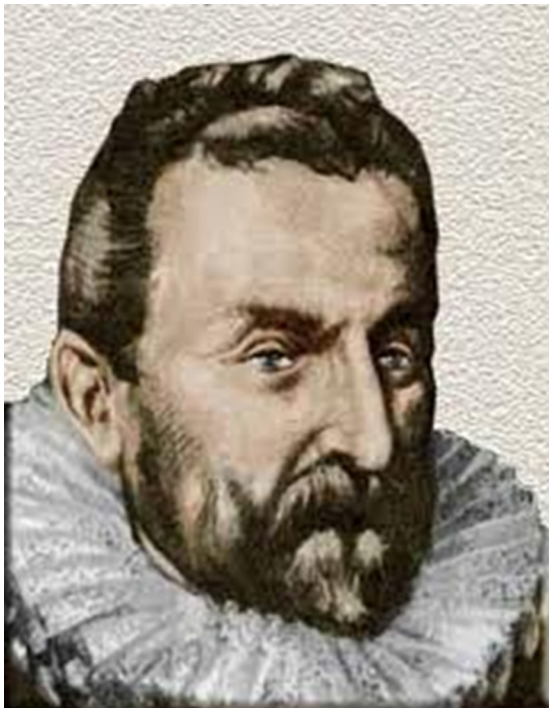

Fig. 2. Jean Nicot.

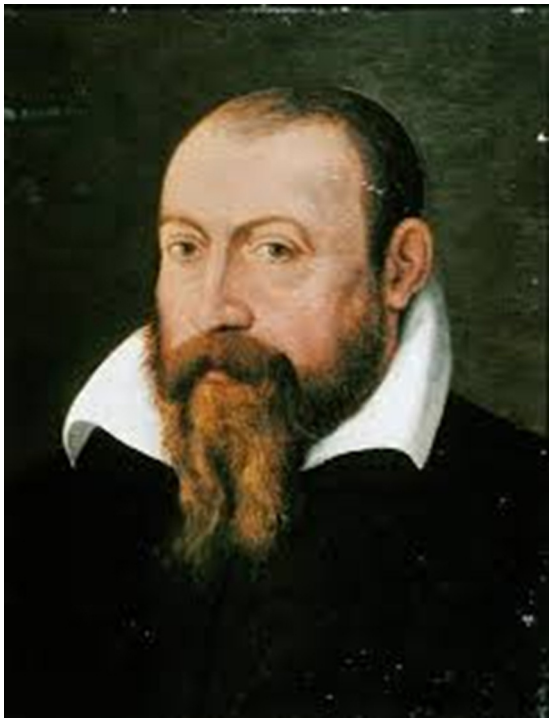

Fig. 3. Jacques Daléchamps.

2. Growth and development

Several factors militated in favor of tobacco's conquest of the world. Initially, its medical reputation was seductive. Add to that the power of fashion and addiction combined with the search for profit on the part of industry and the State did the rest.

A look at the list of the virtues that physicians and men of science at first attributed to tobacco is enough to explain the enthusiasm. Ambroise Paré, for example, recommended local application of the "Catherinary herb" for wounds, and inhalation as a precaution against plague [7]. The physicist René Ferchaud de Réaumur suggested it would be useful in resuscitating victims of drowning, and for Trousseau it had the same properties as solanaceae such as datura inasmuch as he had relieved one of his asthma attacks with a few drags on a cigar [7]. In the field of ENT, Diderot's *Encyclopédie* explained that, in the form of snuff, tobacco "causes an agreeable titillation of the nerves of the pituitary membrane", Voltaire asked "Was tobacco made for the nose or the nose for tobacco?" and Trousseau advised fumigations of tobacco to treat laryngeal phthisis [1,7,8].

Fashion played just as great a role. For courtiers and artists, the use of tobacco was *de rigueur*, and this positive image would last into the mid-19th century. In 1665, in Molière's *Don Juan*, Sganarelle says of tobacco: "It delights the honest man, and whoever lives without tobacco is not worthy of living." Queen Marie-Antoinette's wedding chest contained 52 snuff-boxes (all in gold!), while Frederick I of Prussia founded an Academy of the Pipe [2]. Locke and Newton were both smokers, Johann Sebastian Bach wrote a tobacco cantata, and Kant, Voltaire, Pope, Schiller, Musset, Baudelaire and Georges Sand to name but a few praised the benefits of the herb [2]. Freud later said, "I owe to the cigar a great intensification of my capacity to work and a facilitation of my self-control" [9].

The poor also seized on the herb. Beggars smoked "papelitos": scraps of tobacco rolled up in a vegetable envelope then in paper. This ancestor of the cigarette appeared in the 16th century in Spain and her colonies, and Napoleon's troops adopted it during the Iberian campaign, where their pipes tended to get broken during

the fighting [1,2]. In 1842, in the "*Gros Caillou*" ("Big Stone"!) factory in Paris, the French state tobacco monopoly produced the first real cigarette, five years before Philip Morris set up his first cigarette factory in Oxford and a tobacconist's in London [1,2]. These early cigarettes were hand-made by a female workforce, and productivity was low. Then in 1883 in Richmond, Virginia, James Bonsack slashed costs by inventing, at the age of 18, a machine that could turn out 120,000 cigarettes a day – the equivalent of 48 female factory-hands of the time [1–4]. Nowadays, automated machinery churns out more than 8,000 cigarettes per minute... The geography of manufacture has also shifted: in the early 19th century, 70% of world production was concentrated in the USA; by 2011, this was down to 4%, far behind China's 42% of a worldwide total estimated at some 8 million tons of tobacco leaf [10].

During the 17th century, the Exchequers of Europe quickly developed a taste for the income tobacco could bring in. In Britain, James I introduced a tobacco tax in 1604, although by hiking customs duties by 82 pence per pound he also promoted the cause of smuggling. Even so, he was soon followed by Spain, Venice, the Papal States, the Austrian Empire, Poland and Russia [4]. In France, Richelieu introduced a "duty on *pétun* and tobacco" in 1629 [2]. In 1681, Colbert declared a royal monopoly on what was the largest production in Europe, with plantations in eastern and southwestern France and the French West Indies [2]. The Revolution of 1789 abolished the monopoly and deregulated sale and production [2]. In a Thermidorian reaction, in 1811, Napoleon restored taxation and monopoly [2] – a move which no subsequent French regime was ever to go back on. In 1864, the Civil War gave the American Federal Government a good excuse to fill its coffers with a tobacco tax [4]. Later, in 1921, Iowa introduced the first State tobacco tax, to balance its budget [4]. With the 1929 Crash and the ensuing Depression, all the other States followed suit [4]. The private sector was never far behind: in 2008, with more than a billion smokers worldwide (including more than 15 million in France), 90% of the market was in the hands of 5 companies, 4 of them private, with annual earnings exceeding $300 billion (more than 160 billion of which were handed over to the State) and net profits (after tax) of more than $14 bn [11,12]. According to the World Health Organization, the tobacco industry decided in the 1990s to target emerging countries and the youngest age-groups, investing tens of billions of dollars yearly to do so [13,14].

3. Hazards and conflicts

No sooner was it discovered than tobacco was sparking conflict. In 1498, Columbus's companion Rodrigo de Jerez, who had taken to smoking with the natives, was hauled before the Inquisition for having smoked in public in Barcelona: he was accused of Satanism because of the smoke that came out of his nostrils and was thrown into prison [3]. In England, Henry VIII had smokers whipped and his daughter Elizabeth confiscated pipes and snuff-boxes [2,4]. James I went on to outlaw tobacco-growing and published an anonymous pamphlet entitled *A Counter-Blaste to Tobacco* in which he asked how the brain, being naturally cold and humid, could support inhalation of hot dry smoke, clogging the whole body with its soot. Smoking was a filthy, stinking and ruinous habit, creating a perilous addiction and a drunkenness like that of wine, "loathsome to the eye, hateful to the nose, harmful to the brain, dangerous to the lungs, and in the black stinking fume thereof, nearest resembling the horrible Stygian smoke of the pit that is bottomless" [15]. Sentenced to death by him, Sir Walter Raleigh mounted the scaffold with his Indian pipe in Virginian Maplewood between his lips [1]. The Pope was not to be outdone: in 1642, Urban VII excommunicated several hundred priests who were in the habit of smoking at Mass, as they "sully the sacred cloth with the disgusting humors that tobacco causes and infect our temples with a repugnant odor", and in 1650 all those who "touch the Devil's herb" were threatened with excommunication by Innocent X because cigar and pipe smoke was masking the perfume of the incense and causing certain monks to cough in the middle of hymns [1–3]. In Russia, after a smoker had, in 1634, set off a fire that destroyed many of the wooden houses of Moscow, Tsar Mikhail Fedorovitch Romanov I decreed that dealers should be whipped, smokers caned on the soles of their feet and repeat offenders beheaded [2]. In the East, anti-smoking measures were even more radical. Sultan Murad IV had smokers hanged while Shah Abbas arranged for the punishment to fit the crime, cutting their nose or lips off, and his successor, Saphi, had them impaled, with dealers punished by having molten lead poured down their throats [2]. In Arabia, under Ben-abd-el-Wahad, when a cholera epidemic struck the country, the Wahabites declared it was divine retribution due to tobacco smokers, who were duly massacred in larger numbers than the epidemic itself had accounted for [1].

As tobacco began to be used for non-medical purposes, doubts arose as to its harmlessness. When Jacques Cartier landed on Montreal Island, the Amerindians offered him tobacco; he wrote in his diary, "We tried to imitate them but the smoke burned our mouths as if it had been pepper" [3]. As early as 1659, Dr. Everard was wondering whether this "noble herb" might not also have "the power to shorten our lives" [1]. In 1761, the English physician John Hill published what may be claimed to be the first article implicating tobacco in cancer, *Against the immoderate use of snuff* [3]. In 1681, Simon Paulli, physician to the King of Denmark, claimed in his treatise on the abuse of tobacco and tea that "tobacco when smoked spoils the brain and blackens the skull" [16]. Gui-Crescent Fagon, physician to Louis XIV and protégé of Madame de Maintenon, published around 1710 a memoir entitled *The inconveniences of tobacco*, but unfortunately entrusted the public reading of it to a courtier who was happily sniffing the stuff throughout the presentation! [2,3]. In 1862, the minutes of the *Académie des sciences* mention a case of heart attack following smoke inhalation [1]. Dr Paul Jolly, a member of the French National Academy of Medicine, wrote in 1882 that "Smoking should be ranked at the same level as tuberculosis, alcoholism and syphilis as a scourge of society" [1,17]. Three years later, the French Association Against the Use of Tobacco, of which Pasteur was a member, was founded [1]. Writers took up the cause: Alexandre Dumas (*fils*) declared, "Tobacco in my opinion, together with alcohol, is the most formidable enemy of intelligence, but nothing will destroy the abuse, imbeciles being the most numerous and tobacco having nothing to destroy in them", while according to Balzac "Tobacco destroys the body, damages the mind, and stupefies nations", and for Victor Hugo "Tobacco changes thought into dream. Thought is the labor of the intellect: dream is its pleasure. Woe to him who falls from thoughts into dreams. To replace thought by dreams is to mingle a poison with nourishment" [18]. In the United States, Lucie Page Gaston founded the Anti-Cigarette League of America in December 1899, and Henry Ford became one of its first members [4].

It was during the 20th century that scientific proof of the harmfulness of tobacco accumulated. In 1901, tobacco was designated an "industrial poison" by the French Labor Bureau, and in 1903 the Canadian parliament considered a total ban on cigarettes [3,19]. In the same period, various studies appeared on the dependence and addiction (both of which had actually been described by Sir Francis Bacon in 1623) induced by nicotine [20]. In France, several medical theses denounced the otorhinolaryngologic perils of tobacco [17]. The Great War, however, pushed this into the background: the troops needed cigarettes to keep up their morale [1]. In 1928, in the inter-war years, the *New England Journal of Medicine* reported a cohort of 217 cancer patients, pointing out that those suffering from cancer of the lung, lip, jaw, cheek and to a lesser degree larynx were almost systematically heavy smokers [21]. The medical

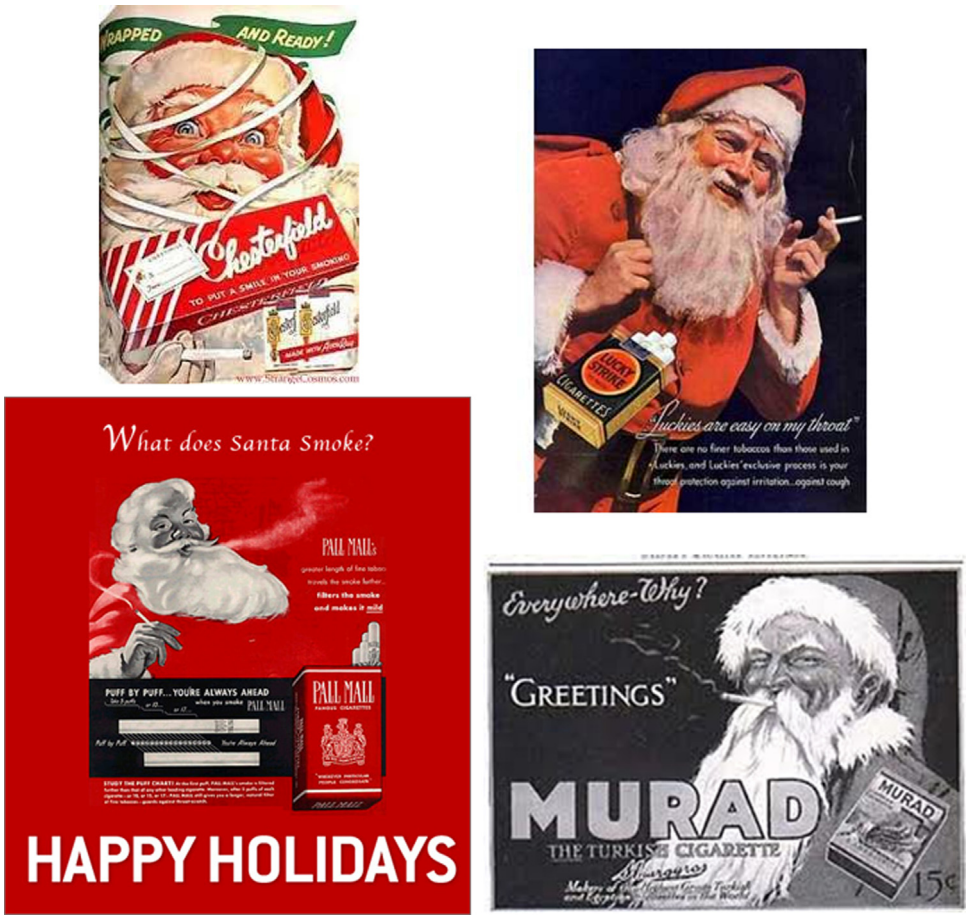

Fig. 4. Tobacco ads.

community's attention was also drawn to the very steep rise in the incidence of lung cancer. While exhaust fumes and asphalt were widely incriminated, in 1939 an American surgeon, Alton Ochsner, published an article implicating smoking [22]. Meanwhile, in Germany, the first epidemiological studies linking lung cancer and smoking were beginning to appear, highlighting the associated vascular complications [23,24]. As a result, in 1942, German women were banned from smoking or buying tobacco and the ration handed out to German soldiers was reduced. In the post-war period, these studies, which had been conducted under the auspices of the Nazi party in a spirit of "racial purification", went discreetly unmentioned. But in 1950 several English-language epidemiological studies relating smoking to lung cancer revived the debate [25–27]. They ran up against a great deal of skepticism promoted by the tobacco companies' intensive lobbying and marketing in favor of the supposed harmlessness of tobacco – going so far as to show Santa Claus with a cigarette (Fig. 4). A pioneer of the anti-smoking campaign, Dr Doll, then decided to undertake a 40-year follow-up study of 40,000 British physicians who smoked, and found that half of them succumbed to their lethal habit [28]. This demonstration was backed up by epidemiological data highlighting an association between smoking and incidence of mortality due to lung cancer, especially in women and including non-smokers whose husbands smoked [4,29]. In 1961, the Kennedy administration set up a Smoking and Health Advisory Committee, whose report formally implicated smoking in the etiology of lung and laryngeal cancer and chronic bronchitis. The American Medical Association, heavily infiltrated by the tobacco industry, took 14 years to come round to these conclusions [4]. In 1969, the Canadian Medical Association acknowledged a causal relationship between smoking and lung cancer [3]. In France, as of the 1970s the National Academy of Medicine published reports formally indicting smoking [1]. Research then began to show that merely passive smoking causes more deaths from cardiac causes than from lung cancer, that the overall risk of death is related to the number of cigarettes smoked per day, and that the mortality risk pattern of smokers who have stopped for at least 10 years is identical to that of non-smokers [1,3,4,29–31]. A range of laws and regulations then began progressively restricting advertising and the public places in which smoking is allowed (not in aircraft, bars, restaurants, high-schools, universities, museums, stations, the work-place, and so on) in Western countries, with campaigns to raise public awareness of the addiction and cause life-threatening diseases that cigarettes cause [1,3,31]. In 1992, the US Food and Drug Administration classified tobacco smoke as being carcinogenic in humans (like radon and asbestos) [3]. And in 1996 Pr Tubiana, a pioneer of French oncology, wrote that "If tobacco were discovered today, it would automatically be banned. That it is used at all is an accident of history" [12].

Although a 1951 ad for a famous brand of cigarettes claimed that they did not "scratch" the throat [3], many studies throughout the 20th century reported the harmful ENT effects of smoking; these are related not to nicotine but to the solid particles (tar) and carbon monoxide released by combustion and which blend within the smoke, causing a variety of smoking-related pathologies (Table 1). More than 50 solid particles (including nitrosamines) found in tobacco smoke constitute risk factors for squamous cell carcinoma not only of the larynx but also of the oral cavity, oropharynx and nasopharynx [32,33]. The pipe-loving Frederick II of Prussia died of throat cancer, as did Puccini, while the cigar-smoking Freud died of

Table 1
Diagrammatic classification of the impact of various tobacco smoke components on the pathological states induced by smoking.

	"Active" combustion products (tars, heavy metals, acrolein, etc.)	Nicotine	"Passive" combustion products (carbon monoxide)	Additives
Addiction	0	+	0	+
Rhinitis, pharyngitis, laryngitis, gingivitis	+	0	0	+
Upper airway and lung cancer	+	0	0	+
Other cancers: stomach, pancreas, bladder, liver, kidney, cervix, colon, prostate, skin	+	0	0	0
Chronic bronchitis	+	+	+	+
Cardiovascular pathologies: angina pectoris, infarction, high blood pressure, heart failure, stroke, aortic aneurysm, arteritis, thromboembolic pathologies	+	+	+	0
Gastro-esophageal reflux, peptic ulcer	+	+	0	0
Skin aging	+	+	+	0
Erectile dysfunction, impaired fertility	+	+	+	0
Osteoporosis	+	+	+	0
Pathologies of pregnancy: ectopic pregnancy, gestational diabetes, preeclampsia, prematurity, hematoma and hemorrhage at delivery, retarded fetal growth	+	+	+	0

+: recognized impact; 0: no recognized impact.

oral cancer. Irritant combustion products (acetone, phenols, hydrocyanic acid) degrade respiratory mucosa and promote upper airway infection, especially in children [3]. Carbon monoxide, formed by incomplete combustion of carbon, has the property of binding onto hemoglobin in the place of oxygen, reducing oxygen levels in the blood and organs; to combat the resulting hypoxia, heart rate and blood pressure increase, reducing effort capacity and increasing cardiovascular risk [3]. In the field of otorhinolaryngology, this vascular involvement impairs a number of sensory functions. For example, recurrence of sudden deafness is more common in smokers [34,35]; so is balance disorder, while smoking counteracts or abolishes the effect of vertigo treatments [36,37]. Finally, smoking damages olfactory nerve endings in the ethmoid; olfactory thresholds are often elevated in smokers, including passive smokers [38]. Likewise, electrogustometric thresholds are elevated: both smell and taste are impaired by smoking.

The medical dangers established by the 21st century (Table 1) are not the only factors weighing in the balance against smoking in Western countries. The tobacco industry's secret archives were thrown open in the lawsuits against the industry in the US, revealing that nicotine concentrations were intentionally adjusted and that some firms resorted to genetically modified tobacco and developed nicotine-elevated strains [3,4]. Moreover, a variety of additives were put in cigarette tobacco and the pH of the smoke was adjusted to increase and accelerate the rush of nicotine to the brain while at the same time making the smoke feel less aggressive, improving the smoker's comfort and thereby enhancing consumption [3,4]. Additives include ammonia, to enhance nicotine absorption, cocoa to dilate the respiratory pathways, and genol and menthol to mask irritation by their soothing properties [3,4]. Independent experts recently analyzed studies ordered by the industry and performed and published in 2002, which claimed that cigarette additives were harmless [39]; in contrast to the industry's published findings, additives in fact significantly increased the addictive and toxic effects of cigarette smoke [39]. On top of such questions of transparency and ethics, there is the ecological issue of how the processing and drying of tobacco leaf contributes to global deforestation and its consequences [3,40]. Governments now realize, moreover, the exorbitant costs smoking incurs for society. In 2012 in France, the national audit office estimated that, while cigarettes bring in €15 billion a year in income, smoking costs society €47 billion, including €12 bn in national health insurance outlay [41]. Likewise in the USA, smoking-related public health costs are estimate at $52 billion, or more than $100 billion if productivity losses are taken into account [3]. Despite sworn statements made by the 17 CEOs of American tobacco multinationals before the House of Representatives in 1994 affirming the harmlessness of tobacco, a Florida jury 2 years later awarded $750,000 to Grady Carter and his wife in a product liability suit against the Brown & Williamson Tobacco Co. [1,3,4]. Fourteen States went on to sue the industry for public health costs implicating smoking [3,4]. In the same year, the tobacco majors were forced into an agreement with the Federal government, guaranteeing their survival up to 2020 in exchange for severe financial penalties [4]. This was only the beginning of a dogged struggle in the American courts against the legal tricks the industry deployed, at great cost to itself, to get round the law [4]. On top of all of these tricks, in 2004, Hon Lik, Chinese pharmacist, invented the electronic cigarette which is presently eating further into the market.

4. Conclusion

Looking at the number of deaths attributable to tobacco during the 20th and early 21st centuries, smoking incontestably emerges as the most lethal epidemic humanity has ever had to face: nearly 6 million deaths per year worldwide – plus whatever assessment can be envisaged of the illnesses and disabilities caused [42]. The voices calling out for the freedom to smoke may be growing fainter, but the financial interests at stake, for industry and all too often for the state, are such that anything goes to keep this hemorrhage of money and human lives flowing. In 2008, governments harvested $167 billion in taxes on tobacco and spent just $965 million on the fight against smoking [1,4]. For these reasons, the international community is not very outspoken when it comes to mortality forecasts for Asia and Africa, where the epidemic will be most devastating in coming years. Some statisticians predict the end of smoking in the West by 2130: in scientific congresses on the fight against smoking, talk of an "end-game" is growing. But will it be the same elsewhere? Cigarette smoking is a scourge the consequences of which outstrip those of all other addictions put together, and respect for individual freedom should not serve as a decoy. As Marc Kirsch put it: "Smoking is not a private matter, and probably never was" [1].

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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